

## SEQUENCE LISTING

<110> Saba, Julie D.  
Fyrst, Henrik

<120> SPHINGOSINE-1-PHOSPHATE LYASE POLYPEPTIDES,  
POLYNUCLEOTIDES AND MODULATING AGENTS AND  
METHODS OF USE THEREFOR

<130> 200116.402C2

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<141> 2002-01-17

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<213> S. cerevisiae

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Ile Leu Thr Ile Asn Glu Leu Lys Ile Ala Ile His Gly Tyr Leu Arg	
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Cys Tyr Lys Leu Ile Ser Asn Phe Phe Tyr Leu Leu Lys Val Tyr Gly	
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Val 180	Arg	Met	Cys	Cys	Asn	Met	Met	Asn	Gly	Asp	Ser	Glu	Thr	Cys	Gly
Thr 195	Met	Ser	Thr	Gly	Gly	Ser	Ile	Ser	Ile	Leu	Leu	Ala	Cys	Leu	Ala
His 210	Arg	Asn	Arg	Leu	Leu	Lys	Arg	Gly	Glu	Lys	Tyr	Thr	Glu	Met	Ile
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Asp 270	Leu	Val	Lys	Met	Lys	Ala	Ala	Ile	Asn	Lys	Arg	Thr	Cys	Met	Leu
Val 285	Gly	Ser	Ala	Pro	Asn	Phe	Pro	Phe	Gly	Thr	Val	Asp	Asp	Ile	Glu
Ala 290	Ile	Gly	Gln	Leu	Gly	Leu	Glu	Tyr	Asp	Ile	Pro	Val	His	Val	Asp
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Arg 320	Tyr	Asp	Phe	Arg	Val	Pro	Gly	Val	Ser	Ser	Ile	Ser	Ala	Asp	Ser
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Gly 485	Leu	Ala	Glu	Ala	Phe	Val	Ala	Asp	Cys	Arg	Ala	Ala	Val	Glu	Phe
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 Glu Ile Leu Glu Ser Tyr Ser Thr Lys Ala Lys Asn Tyr Val Asn Gly  
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tat tgc acc aaa tat gag ccc tgg cag ctc att gcg tgg agt gtc ctg 144  
 Tyr Cys Thr Lys Tyr Glu Pro Trp Gln Leu Ile Ala Trp Ser Val Leu  
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tgt act ctg ctg ata gtc tgg gtg tat gag ctt atc ttc cag cca gag 192  
 Cys Thr Leu Leu Ile Val Trp Val Tyr Glu Leu Ile Phe Gln Pro Glu  
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agt tta tgg tct cgg ttt aaa aaa aaa tta ttt aag ctt atc agg aag 240  
 Ser Leu Trp Ser Arg Phe Lys Lys Lys Leu Phe Lys Leu Ile Arg Lys  
 65 70 75 80

atg cca ttt att gga cgt aag atc gaa caa cag gtg agc aaa gcc aag 288  
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 85 90 95

aag gat ctt gtc aag aac atg cca ttc cta aag gtg gac aag gat tat 336  
 Lys Asp Leu Val Lys Asn Met Pro Phe Leu Lys Val Asp Lys Asp Tyr  
 100 105 110

gtg aaa act ctg cct gct cag ggt atg ggc aca gct gag gtt ctg gag 384  
 Val Lys Thr Leu Pro Ala Gln Gly Met Gly Thr Ala Glu Val Leu Glu  
 115 120 125

aga ctc aag gag tac agc tcc atg gat ggt tcc tgg caa gaa ggg aaa 432  
 Arg Leu Lys Glu Tyr Ser Ser Met Asp Gly Ser Trp Gln Glu Gly Lys  
 130 135 140

gcc tca gga gct gtg tac aat ggg gaa ccg aag ctc acg gag ctg ctg 480  
 Ala Ser Gly Ala Val Tyr Asn Gly Glu Pro Lys Leu Thr Glu Leu Leu  
 145 150 155 160

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tgt tcc ctc ttc aat ggg gga cca gat tcc tgt gga tgt gtg act tct 624  
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ggg gga acg gaa agc atc ctg atg gcc tgc aaa gct tac cgg gac ttg 672  
 Gly Gly Thr Glu Ser Ile Leu Met Ala Cys Lys Ala Tyr Arg Asp Leu  
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gcg tta gag aag ggg atc aaa act cca gaa att gtg gct ccc gag agt 720  
 Ala Leu Glu Lys Gly Ile Lys Thr Pro Glu Ile Val Ala Pro Glu Ser  
 225 230 235 240

gcc cat gct gca ttc gac aaa gca gct cat tat ttt ggg atg aag att 768  
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act gtc aga tat aaa atc cca ctc cat gtg gat gct tgt ctg ggg ggc 960  
 Thr Val Arg Tyr Lys Ile Pro Leu His Val Asp Ala Cys Leu Gly Gly  
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 Phe Asp Phe Arg Val Lys Gly Val Thr Ser Ile Ser Ala Asp Thr His  
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aag tat ggc tat gct cct aaa ggt tca tca gtg gtg atg tac tct aac 1104  
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gag aag tac agg acg tac cag ttc ttt gtt ggt gca gac tgg caa ggt 1152  
 Glu Lys Tyr Arg Thr Tyr Gln Phe Phe Val Gly Ala Asp Trp Gln Gly  
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1055310 0103

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 Ile Ala Ala Cys Trp Ala Ala Leu Met His Phe Gly Glu Asn Gly Tyr  
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 gtt gaa gct acc aaa cag atc atc aaa act gct cgc ttc ctg aag tca 1296  
 Val Glu Ala Thr Lys Gln Ile Ile Lys Thr Ala Arg Phe Leu Lys Ser  
 420 425 430  
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 Glu Leu Glu Asn Ile Lys Asn Ile Phe Ile Phe Gly Asp Pro Gln Leu  
 435 440 445  
 tca gtt att gct ctg gga tcc aac gat ttt gac att tac cga cta tct 1392  
 Ser Val Ile Ala Leu Gly Ser Asn Asp Phe Asp Ile Tyr Arg Leu Ser  
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 aat atg atg tct gct aag ggg tgg aat ttt aac tac ctg cag ttc cca 1440  
 Asn Met Met Ser Ala Lys Gly Trp Asn Phe Asn Tyr Leu Gln Phe Pro  
 465 470 475 480  
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 485 490 495  
 gcg atc cag ttc cta aag gat atc cgg gaa tca gtc aca caa atc atg 1536  
 Ala Ile Gln Phe Leu Lys Asp Ile Arg Glu Ser Val Thr Gln Ile Met  
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 Lys Asn Pro Lys Ala Lys Thr Thr Gly Met Gly Ala Ile Tyr Gly Met  
 515 520 525  
 gcc cag gca acc att gac agg aag ctg gtt gca gaa ata tcc tcc gtc 1632  
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 Cys Thr Leu Leu Ile Val Trp Val Tyr Glu Leu Ile Phe Gln Pro Glu  
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 Ser Leu Trp Ser Arg Phe Lys Lys Lys Leu Phe Lys Leu Ile Arg Lys  
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 Met Pro Phe Ile Gly Arg Lys Ile Glu Gln Gln Val Ser Lys Ala Lys  
 85 90 95  
 Lys Asp Leu Val Lys Asn Met Pro Phe Leu Lys Val Asp Lys Asp Tyr  
 100 105 110  
 Val Lys Thr Leu Pro Ala Gln Gly Met Gly Thr Ala Glu Val Leu Glu  
 115 120 125  
 Arg Leu Lys Glu Tyr Ser Ser Met Asp Gly Ser Trp Gln Glu Gly Lys  
 130 135 140  
 Ala Ser Gly Ala Val Tyr Asn Gly Glu Pro Lys Leu Thr Glu Leu Leu  
 145 150 155 160  
 Val Gln Ala Tyr Gly Glu Phe Thr Trp Ser Asn Pro Leu His Pro Asp  
 165 170 175  
 Ile Phe Pro Gly Leu Arg Lys Leu Glu Ala Glu Ile Val Arg Met Thr  
 180 185 190  
 Cys Ser Leu Phe Asn Gly Gly Pro Asp Ser Cys Gly Cys Val Thr Ser  
 195 200 205  
 Gly Gly Thr Glu Ser Ile Leu Met Ala Cys Lys Ala Tyr Arg Asp Leu  
 210 215 220  
 Ala Leu Glu Lys Gly Ile Lys Thr Pro Glu Ile Val Ala Pro Glu Ser  
 225 230 235 240  
 Ala His Ala Ala Phe Asp Lys Ala Ala His Tyr Phe Gly Met Lys Ile  
 245 250 255  
 Val Arg Val Ala Leu Lys Lys Asn Met Glu Val Asp Val Gln Ala Met  
 260 265 270  
 Lys Arg Ala Ile Ser Arg Asn Thr Ala Met Leu Val Cys Ser Thr Pro  
 275 280 285  
 Gln Phe Pro His Gly Val Met Asp Pro Val Pro Glu Val Ala Lys Leu  
 290 295 300  
 Thr Val Arg Tyr Lys Ile Pro Leu His Val Asp Ala Cys Leu Gly Gly  
 305 310 315 320  
 Phe Leu Ile Val Phe Met Glu Lys Ala Gly Tyr Pro Leu Glu Lys Pro  
 325 330 335  
 Phe Asp Phe Arg Val Lys Gly Val Thr Ser Ile Ser Ala Asp Thr His  
 340 345 350  
 Lys Tyr Gly Tyr Ala Pro Lys Gly Ser Ser Val Val Met Tyr Ser Asn  
 355 360 365  
 Glu Lys Tyr Arg Thr Tyr Gln Phe Phe Val Gly Ala Asp Trp Gln Gly  
 370 375 380  
 Gly Val Tyr Ala Ser Pro Ser Ile Ala Gly Ser Arg Pro Gly Gly Ile  
 385 390 395 400  
 Ile Ala Ala Cys Trp Ala Ala Leu Met His Phe Gly Glu Asn Gly Tyr  
 405 410 415  
 Val Glu Ala Thr Lys Gln Ile Ile Lys Thr Ala Arg Phe Leu Lys Ser  
 420 425 430

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Glu Leu Glu Asn Ile Lys Asn Ile Phe Ile Phe Gly Asp Pro Gln Leu  
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 Ser Val Ile Ala Leu Gly Ser Asn Asp Phe Asp Ile Tyr Arg Leu Ser  
           450                          455                          460  
 Asn Met Met Ser Ala Lys Gly Trp Asn Phe Asn Tyr Leu Gln Phe Pro  
 465                          470                          475                          480  
 Arg Ser Ile His Phe Cys Ile Thr Leu Val His Thr Arg Lys Arg Val  
                           485                          490                          495  
 Ala Ile Gln Phe Leu Lys Asp Ile Arg Glu Ser Val Thr Gln Ile Met  
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 Lys Asn Pro Lys Ala Lys Thr Thr Gly Met Gly Ala Ile Tyr Gly Met  
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 Ala Gln Ala Thr Ile Asp Arg Lys Leu Val Ala Glu Ile Ser Ser Val  
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 Phe Leu Asp Cys Leu Tyr Thr Thr Asp Pro Val Thr Gln Gly Asn Gln  
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 gag att ttg gaa gta tac tcc aca aaa gcc aag aat tat gta aat gga 96  
 Glu Ile Leu Glu Val Tyr Ser Thr Lys Ala Lys Asn Tyr Val Asn Gly  
           20                          25                          30  
  
 cat tgc acc aag tat gag ccc tgg cag cta att gca tgg agt gtc gtg 144  
 His Cys Thr Lys Tyr Glu Pro Trp Gln Leu Ile Ala Trp Ser Val Val  
           35                          40                          45  
  
 tgg acc ctg ctg ata gtc tgg gga tat gag ttt gtc ttc cag cca gag 192  
 Trp Thr Leu Leu Ile Val Trp Gly Tyr Glu Phe Val Phe Gln Pro Glu  
           50                          55                          60  
  
 agt tta tgg tca agg ttt aaa aag aaa tgt ttt aag ctc acc agg aag 240  
 Ser Leu Trp Ser Arg Phe Lys Lys Lys Cys Phe Lys Leu Thr Arg Lys  
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 atg ccc att att ggt cgt aag att caa gac aag ttg aac aag acc aag 288  
 Met Pro Ile Ile Gly Arg Lys Ile Gln Asp Lys Leu Asn Lys Thr Lys  
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gtg aaa gct tta ccc tcc cag ggt ctg agc tca tct gct gtt ttg gag 384  
Val Lys Ala Leu Pro Ser Gln Gly Leu Ser Ser Ser Ala Val Leu Glu  
115 120 125

aaa ctt aag gag tac agc tct atg gac gcc ttc tgg caa gag ggg aga 432  
Lys Leu Lys Glu Tyr Ser Ser Met Asp Ala Phe Trp Gln Glu Gly Arg  
130 135 140

gcc tct gga aca gtg tac agt ggg gag gag aag ctc act gag ctc ctt 480  
Ala Ser Gly Thr Val Tyr Ser Gly Glu Glu Lys Leu Thr Glu Leu Leu  
145 150 155 160

gtg aag gct tat gga gat ttt gca tgg agt aac ccc ctg cat cca gat 528  
Val Lys Ala Tyr Gly Asp Phe Ala Trp Ser Asn Pro Leu His Pro Asp  
165 170 175

atc ttc cca gga cta cgc aag ata gag gca gaa att gtg agg ata gct 576  
Ile Phe Pro Gly Leu Arg Lys Ile Glu Ala Glu Ile Val Arg Ile Ala  
180 185 190

tgt tcc ctg ttc aat ggg gga cca gat tcg tgt gga tgt gtg act tct 624  
Cys Ser Leu Phe Asn Gly Gly Pro Asp Ser Cys Gly Cys Val Thr Ser  
195 200 205

ggg gga aca gaa agc ata ctc atg gcc tgc aaa gca tgt cgg gat ctg 672  
Gly Gly Thr Glu Ser Ile Leu Met Ala Cys Lys Ala Cys Arg Asp Leu  
210 215 220

gcc ttt gag aag ggg atc aaa act cca gaa att gtg gct ccc caa agt 720  
Ala Phe Glu Lys Gly Ile Lys Thr Pro Glu Ile Val Ala Pro Gln Ser  
225 230 235 240

gcc cat gct gca ttt aac aaa gca gcc agt tac ttt ggg atg aag att 768  
Ala His Ala Ala Phe Asn Lys Ala Ala Ser Tyr Phe Gly Met Lys Ile  
245 250 255

gtg cgg gtc cca ttg acg aag atg atg gag gtg gat gtg agg gca atg 816  
Val Arg Val Pro Leu Thr Lys Met Met Glu Val Asp Val Arg Ala Met  
260 265 270

aga aga gct atc tcc agg aac act gcc atg ctc gtc tgt tct acc cca 864  
Arg Arg Ala Ile Ser Arg Asn Thr Ala Met Leu Val Cys Ser Thr Pro  
275 280 285

cag ttt cct cat ggt gta ata gat cct gtc cct gaa gtg gcc aag ctg 912  
Gln Phe Pro His Gly Val Ile Asp Pro Val Pro Glu Val Ala Lys Leu  
290 295 300

gct gtc aaa tac aaa ata ccc ctt cat gtc gac gct tgt ctg gga ggc 960  
Ala Val Lys Tyr Lys Ile Pro Leu His Val Asp Ala Cys Leu Gly Gly

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202770 015500

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Phe Leu Ile Val Phe Met Glu Lys Ala Gly Tyr Pro Leu Glu His Pro				
325	330	335		
ttt gat ttc cgg gtg aaa ggt gta acc agc att tca gct gac acc cat	1056			
Phe Asp Phe Arg Val Lys Gly Val Thr Ser Ile Ser Ala Asp Thr His				
340	345	350		
aag tat ggc tat gcc cca aaa ggc tca tca ttg gtg ttg tat agt gac	1104			
Lys Tyr Gly Tyr Ala Pro Lys Gly Ser Ser Leu Val Leu Tyr Ser Asp				
355	360	365		
aag aag tac agg aac tat cag ttc ttc gtc gat aca gat tgg cag ggt	1152			
Lys Lys Tyr Arg Asn Tyr Gln Phe Phe Val Asp Thr Asp Trp Gln Gly				
370	375	380		
ggc atc tat gct tcc cca acc atc gca ggc tca cgg cct ggt ggc att	1200			
Gly Ile Tyr Ala Ser Pro Thr Ile Ala Gly Ser Arg Pro Gly Gly Ile				
385	390	395	400	
agc gca gcc tgt tgg gct gcc ttg atg cac ttc ggt gag aac ggc tat	1248			
Ser Ala Ala Cys Trp Ala Ala Leu Met His Phe Gly Glu Asn Gly Tyr				
405	410	415		
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Val Glu Ala Thr Lys Gln Ile Ile Lys Thr Ala Arg Phe Leu Lys Ser				
420	425	430		
gaa ctg gaa aat atc aaa ggc atc ttt gtt ttt ggg aat ccc caa ttg	1344			
Glu Leu Glu Asn Ile Lys Gly Ile Phe Val Phe Gly Asn Pro Gln Leu				
435	440	445		
tca ctc att gct ctg gga tcc cgt gat ttt gac atc tac cga cta tca	1392			
Ser Leu Ile Ala Leu Gly Ser Arg Asp Phe Asp Ile Tyr Arg Leu Ser				
450	455	460		
aac ctg atg act gct aag ggg tgg aac ttg aac cag ttg cag ttc cca	1440			
Asn Leu Met Thr Ala Lys Gly Trp Asn Leu Asn Gln Leu Gln Phe Pro				
465	470	475	480	
ccc agt att cat ttc tgc atc aca tta cta cac gcc cgg aaa cga gta	1488			
Pro Ser Ile His Phe Cys Ile Thr Leu Leu His Ala Arg Lys Arg Val				
485	490	495		
gct ata caa ttc cta aag gac att cga gaa tct gtc act caa atc atg	1536			
Ala Ile Gln Phe Leu Lys Asp Ile Arg Glu Ser Val Thr Gln Ile Met				
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aag aat cct aaa gcg aag acc aca gga atg ggt gcc atc tat gcc atg	1584			
Lys Asn Pro Lys Ala Lys Thr Thr Gly Met Gly Ala Ile Tyr Ala Met				
515	520	525		

1055510 04402



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ttc ttg gac agc ttg tac agc acc gac act gtc acc cag ggc agc cag 1680  
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 His Cys Thr Lys Tyr Glu Pro Trp Gln Leu Ile Ala Trp Ser Val Val  
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 Trp Thr Leu Leu Ile Val Trp Gly Tyr Glu Phe Val Phe Gln Pro Glu  
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 Met Pro Ile Ile Gly Arg Lys Ile Gln Asp Lys Leu Asn Lys Thr Lys  
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 Asp Asp Ile Ser Lys Asn Met Ser Phe Leu Lys Val Asp Lys Glu Tyr  
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 Lys Leu Lys Glu Tyr Ser Ser Met Asp Ala Phe Trp Gln Glu Gly Arg  
           130                          135                          140  
 Ala Ser Gly Thr Val Tyr Ser Gly Glu Glu Lys Leu Thr Glu Leu Leu  
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 Val Lys Ala Tyr Gly Asp Phe Ala Trp Ser Asn Pro Leu His Pro Asp  
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 Ile Phe Pro Gly Leu Arg Lys Ile Glu Ala Glu Ile Val Arg Ile Ala  
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 Cys Ser Leu Phe Asn Gly Gly Pro Asp Ser Cys Gly Cys Val Thr Ser  
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 Gly Gly Thr Glu Ser Ile Leu Met Ala Cys Lys Ala Cys Arg Asp Leu  
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 Ala His Ala Ala Phe Asn Lys Ala Ala Ser Tyr Phe Gly Met Lys Ile  
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275 280 285  
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 Phe Asp Phe Arg Val Lys Gly Val Thr Ser Ile Ser Ala Asp Thr His  
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 Lys Tyr Gly Tyr Ala Pro Lys Gly Ser Ser Leu Val Leu Tyr Ser Asp  
 355 360 365  
 Lys Lys Tyr Arg Asn Tyr Gln Phe Phe Val Asp Thr Asp Trp Gln Gly  
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 385 390 395 400  
 Ser Ala Ala Cys Trp Ala Ala Leu Met His Phe Gly Glu Asn Gly Tyr  
 405 410 415  
 Val Glu Ala Thr Lys Gln Ile Ile Lys Thr Ala Arg Phe Leu Lys Ser  
 420 425 430  
 Glu Leu Glu Asn Ile Lys Gly Ile Phe Val Phe Gly Asn Pro Gln Leu  
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 Ser Leu Ile Ala Leu Gly Ser Arg Asp Phe Asp Ile Tyr Arg Leu Ser  
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 Asn Leu Met Thr Ala Lys Gly Trp Asn Leu Asn Gln Leu Gln Phe Pro  
 465 470 475 480  
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 485 490 495  
 Ala Ile Gln Phe Leu Lys Asp Ile Arg Glu Ser Val Thr Gln Ile Met  
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 Lys Asn Pro Lys Ala Lys Thr Thr Gly Met Gly Ala Ile Tyr Ala Met  
 515 520 525  
 Ala Gln Thr Thr Val Asp Arg Asn Met Val Ala Glu Leu Ser Ser Val  
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 gag att ttg gaa gta tac tcc aca aaa gcc aag aat tat gta aat gga 96

Glu	Ile	Leu	Glu	Val	Tyr	Ser	Thr	Lys	Ala	Lys	Asn	Tyr	Val	Asn	Gly		
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cat	tgc	acc	aag	tat	gag	ccc	tgg	cag	cta	att	gca	tgg	agt	gtc	gtg	144	
His	Cys	Thr	Lys	Tyr	Glu	Pro	Trp	Gln	Leu	Ile	Ala	Trp	Ser	Val	Val		
		35					40				45						
tgg	acc	ctg	ctg	ata	gtc	tgg	gga	tat	gag	ttt	gtc	ttc	cag	cca	gag	192	
Trp	Thr	Leu	Leu	Ile	Val	Trp	Gly	Tyr	Glu	Phe	Val	Phe	Gln	Pro	Glu		
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agt	tta	tgg	tca	agg	ttt	aaa	aag	aaa	tgt	ttt	aag	ctc	acc	agg	aag	240	
Ser	Leu	Trp	Ser	Arg	Phe	Lys	Lys	Lys	Cys	Phe	Lys	Leu	Thr	Arg	Lys		
65				70					75						80		
atg	ccc	att	att	ggg	cgt	aag	att	caa	gac	aag	ttg	aac	aag	acc	aag	288	
Met	Pro	Ile	Ile	Gly	Arg	Lys	Ile	Gln	Asp	Lys	Leu	Asn	Lys	Thr	Lys		
				85				90						95			
gat	gat	att	agc	aag	aac	atg	tca	ttc	ctg	aaa	gtg	gac	aaa	gag	tat	336	
Asp	Asp	Ile	Ser	Lys	Asn	Met	Ser	Phe	Leu	Lys	Val	Asp	Lys	Glu	Tyr		
		100						105					110				
gtg	aaa	gct	tta	ccc	tcc	cag	ggg	ctg	agc	tca	tct	gct	ggt	ttg	gag	384	
Val	Lys	Ala	Leu	Pro	Ser	Gln	Gly	Leu	Ser	Ser	Ser	Ala	Val	Leu	Glu		
	115					120						125					
aaa	ctt	aag	gag	tac	agc	tct	atg	gac	gcc	ttc	tgg	caa	gag	ggg	aga	432	
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 gag att ttg gaa gta tac tcc aca aaa gcc aag aat tat gta aat gga 96  
 Glu Ile Leu Glu Val Tyr Ser Thr Lys Ala Lys Asn Tyr Val Asn Gly  
 20 25 30  
 cat tgc acc aag tat gag ccc tgg cag cta att gca tgg agt gtc gtg 144  
 His Cys Thr Lys Tyr Glu Pro Trp Gln Leu Ile Ala Trp Ser Val Val  
 35 40 45  
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Trp	Thr	Leu	Leu	Ile	Val	Trp	Gly	Tyr	Glu	Phe	Val	Phe	Gln	Pro	Glu	
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Ser	Leu	Trp	Ser	Arg	Phe	Lys	Lys	Lys	Cys	Phe	Lys	Leu	Thr	Arg	Lys	
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atg	ccc	att	att	ggg	cgt	aag	att	caa	gac	aag	ttg	aac	aag	acc	aag	288
Met	Pro	Ile	Ile	Gly	Arg	Lys	Ile	Gln	Asp	Lys	Leu	Asn	Lys	Thr	Lys	
				85					90						95	
gat	gat	att	agc	aag	aac	atg	tca	ttc	ctg	aaa	gtg	gac	aaa	gag	tat	336
Asp	Asp	Ile	Ser	Lys	Asn	Met	Ser	Phe	Leu	Lys	Val	Asp	Lys	Glu	Tyr	
			100					105					110			
gtg	aaa	gct	tta	ccc	tcc	cag	ggg	ctg	agc	tca	tct	gct	gtt	ttg	gag	384
Val	Lys	Ala	Leu	Pro	Ser	Gln	Gly	Leu	Ser	Ser	Ser	Ala	Val	Leu	Glu	
	115						120					125				
aaa	ctt	aag	gag	tac	agc	tct	atg	gac	gcc	ttc	tgg	caa	gag	ggg	aga	432
Lys	Leu	Lys	Glu	Tyr	Ser	Ser	Met	Asp	Ala	Phe	Trp	Gln	Glu	Gly	Arg	
	130						135				140					
gcc	tct	gga	aca	gtg	tac	agt	ggg	gag	gag	aag	ctc	act	gag	ctc	ctt	480
Ala	Ser	Gly	Thr	Val	Tyr	Ser	Gly	Glu	Glu	Lys	Leu	Thr	Glu	Leu	Leu	
145					150					155					160	
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Val	Lys	Ala	Tyr	Gly	Asp	Phe	Ala	Trp	Ser	Asn	Pro	Leu	His	Pro	Asp	
				165				170						175		
atc	ttc	cca	gga	cta	cgc	aag	ata	gag	gca	gaa	att	gtg	agg	ata	gct	576
Ile	Phe	Pro	Gly	Leu	Arg	Lys	Ile	Glu	Ala	Glu	Ile	Val	Arg	Ile	Ala	
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tgt	tcc	ctg	ttc	aat	ggg	gga	cca	gat	tcg	tgt	gga	tgt	gtg	act	tct	624
Cys	Ser	Leu	Phe	Asn	Gly	Gly	Pro	Asp	Ser	Cys	Gly	Cys	Val	Thr	Ser	
	195						200					205				
ggg	gga	aca	gaa	agc	ata	ctc	atg	gcc	tgc	aaa	gca	tat	cgg	gat	ctg	672
Gly	Gly	Thr	Glu	Ser	Ile	Leu	Met	Ala	Cys	Lys	Ala	Tyr	Arg	Asp	Leu	
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gcc	ttt	gag	aag	ggg	atc	aaa	act	cca	gaa	att	gtg	gct	ccc	caa	agt	720
Ala	Phe	Glu	Lys	Gly	Ile	Lys	Thr	Pro	Glu	Ile	Val	Ala	Pro	Gln	Ser	
225					230					235					240	
gcc	cat	gct	gca	ttt	aac	aaa	gca	gcc	agt	tac	ttt	ggg	atg	aag	att	768
Ala	His	Ala	Ala	Phe	Asn	Lys	Ala	Ala	Ser	Tyr	Phe	Gly	Met	Lys	Ile	
				245					250					255		
gtg	cgg	gtc	cca	ttg	acg	aag	atg	atg	gag	gtg	gat	gtg	agg	gca	atg	816
Val	Arg	Val	Pro	Leu	Thr	Lys	Met	Met	Glu	Val	Asp	Val	Arg	Ala	Met	
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Arg	Arg	Ala	Ile	Ser	Arg	Asn	Thr	Ala	Met	Leu	Val	Cys	Ser	Thr	Pro	
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cag	ttt	cct	cat	ggg	gta	ata	gat	cct	gtc	cct	gaa	gtg	gcc	aag	ctg	912
Gln	Phe	Pro	His	Gly	Val	Ile	Asp	Pro	Val	Pro	Glu	Val	Ala	Lys	Leu	
	290					295					300					
gct	gtc	aaa	tac	aaa	ata	ccc	ctt	cat	gtc	gac	gct	tgt	ctg	gga	ggc	960
Ala	Val	Lys	Tyr	Lys	Ile	Pro	Leu	His	Val	Asp	Ala	Cys	Leu	Gly	Gly	
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ttc	ctc	atc	gtc	ttt	atg	gag	aaa	gca	gga	tac	cca	ctg	gag	cac	cca	1008
Phe	Leu	Ile	Val	Phe	Met	Glu	Lys	Ala	Gly	Tyr	Pro	Leu	Glu	His	Pro	
				325					330					335		
ttt	gat	ttc	cgg	gtg	aaa	ggg	gta	acc	agc	att	tca	gct	gac	acc	cat	1056
Phe	Asp	Phe	Arg	Val	Lys	Gly	Val	Thr	Ser	Ile	Ser	Ala	Asp	Thr	His	
			340					345					350			
aag	tat	ggc	tat	gcc	cca	aaa	ggc	tca	tca	ttg	gtg	ttg	tat	agt	gac	1104
Lys	Tyr	Gly	Tyr	Ala	Pro	Lys	Gly	Ser	Ser	Leu	Val	Leu	Tyr	Ser	Asp	
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Lys	Lys	Tyr	Arg	Asn	Tyr	Gln	Phe	Phe	Val	Asp	Thr	Asp	Trp	Gln	Gly	
		370				375					380					
ggc	atc	tat	gct	tcc	cca	acc	atc	gca	ggc	tca	cgg	cct	ggg	ggc	att	1200
Gly	Ile	Tyr	Ala	Ser	Pro	Thr	Ile	Ala	Gly	Ser	Arg	Pro	Gly	Gly	Ile	
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agc	gca	gcc	tgt	tgg	gct	gcc	ttg	atg	cac	ttc	ggg	gag	aac	ggc	tat	1248
Ser	Ala	Ala	Cys	Trp	Ala	Ala	Leu	Met	His	Phe	Gly	Glu	Asn	Gly	Tyr	
				405					410					415		
gtt	gaa	gct	acc	aaa	cag	atc	atc	aaa	act	gct	cgc	ttc	ctc	aag	tca	1296
Val	Glu	Ala	Thr	Lys	Gln	Ile	Ile	Lys	Thr	Ala	Arg	Phe	Leu	Lys	Ser	
			420					425					430			
gaa	ctg	gaa	aat	atc	aaa	ggc	atc	ttt	gtt	ttt	ggg	aat	ccc	caa	ttg	1344
Glu	Leu	Glu	Asn	Ile	Lys	Gly	Ile	Phe	Val	Phe	Gly	Asn	Pro	Gln	Leu	
		435					440					445				
tca	gtc	att	gct	ctg	gga	tcc	cgt	gat	ttt	gac	atc	tac	cga	cta	tca	1392
Ser	Val	Ile	Ala	Leu	Gly	Ser	Arg	Asp	Phe	Asp	Ile	Tyr	Arg	Leu	Ser	
		450				455					460					
aac	ctg	atg	act	gct	aag	ggg	tgg	aac	ttg	aac	cag	ttg	cag	ttc	cca	1440
Asn	Leu	Met	Thr	Ala	Lys	Gly	Trp	Asn	Leu	Asn	Gln	Leu	Gln	Phe	Pro	
465					470					475					480	
ccc	agt	att	cat	ttc	tgc	atc	aca	tta	cta	cac	gcc	cgg	aaa	cga	gta	1488

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Pro Ser Ile His Phe Cys Ile Thr Leu Leu His Ala Arg Lys Arg Val  
                   485                                  490                                  495

gct ata caa ttc cta aag gac att cga gaa tct gtc act caa atc atg 1536  
 Ala Ile Gln Phe Leu Lys Asp Ile Arg Glu Ser Val Thr Gln Ile Met  
                   500                                  505                                  510

aag aat cct aaa gcg aag acc aca gga atg ggt gcc atc tat ggc atg 1584  
 Lys Asn Pro Lys Ala Lys Thr Thr Gly Met Gly Ala Ile Tyr Gly Met  
                   515                                  520                                  525

gcc cag aca act gtt gac agg aat atg gtt gca gaa ttg tcc tca gtc 1632  
 Ala Gln Thr Thr Val Asp Arg Asn Met Val Ala Glu Leu Ser Ser Val  
                   530                                  535                                  540

ttc ttg gac agc ttg tac agc acc gac act gtc acc cag ggc agc cag 1680  
 Phe Leu Asp Ser Leu Tyr Ser Thr Asp Thr Val Thr Gln Gly Ser Gln  
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atg aat ggt tct cca aaa ccc cac tga 1707  
 Met Asn Gly Ser Pro Lys Pro His \*  
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                   20                                  25                                  30  
 His Cys Thr Lys Tyr Glu Pro Trp Gln Leu Ile Ala Trp Ser Val Val  
                   35                                  40                                  45  
 Trp Thr Leu Leu Ile Val Trp Gly Tyr Glu Phe Val Phe Gln Pro Glu  
                   50                                  55                                  60  
 Ser Leu Trp Ser Arg Phe Lys Lys Lys Cys Phe Lys Leu Thr Arg Lys  
   65                  70                                  75                                  80  
 Met Pro Ile Ile Gly Arg Lys Ile Gln Asp Lys Leu Asn Lys Thr Lys  
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 Asp Asp Ile Ser Lys Asn Met Ser Phe Leu Lys Val Asp Lys Glu Tyr  
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 Val Lys Ala Leu Pro Ser Gln Gly Leu Ser Ser Ser Ala Val Leu Glu  
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 Lys Leu Lys Glu Tyr Ser Ser Met Asp Ala Phe Trp Gln Glu Gly Arg  
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 Ala Ser Gly Thr Val Tyr Ser Gly Glu Glu Lys Leu Thr Glu Leu Leu  
   145                  150                                  155                                  160  
 Val Lys Ala Tyr Gly Asp Phe Ala Trp Ser Asn Pro Leu His Pro Asp  
                   165                                  170                                  175  
 Ile Phe Pro Gly Leu Arg Lys Ile Glu Ala Glu Ile Val Arg Ile Ala  
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Cys Ser Leu Phe Asn Gly Gly Pro Asp Ser Cys Gly Cys Val Thr Ser  
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 Gly Gly Thr Glu Ser Ile Leu Met Ala Cys Lys Ala Tyr Arg Asp Leu  
 210 215 220  
 Ala Phe Glu Lys Gly Ile Lys Thr Pro Glu Ile Val Ala Pro Gln Ser  
 225 230 235 240  
 Ala His Ala Ala Phe Asn Lys Ala Ala Ser Tyr Phe Gly Met Lys Ile  
 245 250 255  
 Val Arg Val Pro Leu Thr Lys Met Met Glu Val Asp Val Arg Ala Met  
 260 265 270  
 Arg Arg Ala Ile Ser Arg Asn Thr Ala Met Leu Val Cys Ser Thr Pro  
 275 280 285  
 Gln Phe Pro His Gly Val Ile Asp Pro Val Pro Glu Val Ala Lys Leu  
 290 295 300  
 Ala Val Lys Tyr Lys Ile Pro Leu His Val Asp Ala Cys Leu Gly Gly  
 305 310 315 320  
 Phe Leu Ile Val Phe Met Glu Lys Ala Gly Tyr Pro Leu Glu His Pro  
 325 330 335  
 Phe Asp Phe Arg Val Lys Gly Val Thr Ser Ile Ser Ala Asp Thr His  
 340 345 350  
 Lys Tyr Gly Tyr Ala Pro Lys Gly Ser Ser Leu Val Leu Tyr Ser Asp  
 355 360 365  
 Lys Lys Tyr Arg Asn Tyr Gln Phe Phe Val Asp Thr Asp Trp Gln Gly  
 370 375 380  
 Gly Ile Tyr Ala Ser Pro Thr Ile Ala Gly Ser Arg Pro Gly Gly Ile  
 385 390 395 400  
 Ser Ala Ala Cys Trp Ala Ala Leu Met His Phe Gly Glu Asn Gly Tyr  
 405 410 415  
 Val Glu Ala Thr Lys Gln Ile Ile Lys Thr Ala Arg Phe Leu Lys Ser  
 420 425 430  
 Glu Leu Glu Asn Ile Lys Gly Ile Phe Val Phe Gly Asn Pro Gln Leu  
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 Ser Val Ile Ala Leu Gly Ser Arg Asp Phe Asp Ile Tyr Arg Leu Ser  
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 Asn Leu Met Thr Ala Lys Gly Trp Asn Leu Asn Gln Leu Gln Phe Pro  
 465 470 475 480  
 Pro Ser Ile His Phe Cys Ile Thr Leu Leu His Ala Arg Lys Arg Val  
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 Ala Ile Gln Phe Leu Lys Asp Ile Arg Glu Ser Val Thr Gln Ile Met  
 500 505 510  
 Lys Asn Pro Lys Ala Lys Thr Thr Gly Met Gly Ala Ile Tyr Gly Met  
 515 520 525  
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Trp	His	His	Thr	Ile	Arg	Lys	His	Lys	Arg	Gly	Asn	Gly	Ser	Ser	Ser
			20					25					30		
Pro	Ala	Asp	Cys	Gly	Lys	Gln	Leu	Leu	Ile	Leu	Leu	Asn	Pro	Lys	Ser
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Gly	Ser	Gly	Lys	Gly	Arg	Glu	Leu	Phe	Gln	Lys	Gln	Val	Ala	Pro	Leu
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Leu	Thr	Glu	Ala	Glu	Val	Gln	Tyr	Asp	Leu	Gln	Ile	Thr	Thr	His	Pro
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Gln	Tyr	Ala	Lys	Glu	Phe	Val	Arg	Thr	Arg	Arg	Asp	Leu	Leu	Thr	Arg
				85					90					95	
Tyr	Ser	Gly	Ile	Val	Val	Ala	Ser	Gly	Asp	Gly	Leu	Phe	Tyr	Glu	Val
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Leu	Asn	Gly	Leu	Met	Glu	Arg	Met	Asp	Trp	Arg	Arg	Ala	Cys	Arg	Glu
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Leu	Pro	Leu	Gly	Ile	Ile	Pro	Cys	Gly	Ser	Gly	Asn	Gly	Leu	Ala	Lys
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Ser	Val	Ala	His	His	Cys	Asn	Glu	Pro	Tyr	Glu	Pro	Lys	Pro	Ile	Leu
145					150					155					160
His	Ala	Thr	Leu	Thr	Cys	Met	Ala	Gly	Lys	Ser	Thr	Pro	Met	Asp	Val
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Val	Arg	Val	Glu	Leu	Ala	Thr	Arg	Asp	Lys	His	Phe	Val	Met	Tyr	Ser
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Phe	Leu	Ser	Val	Gly	Trp	Gly	Leu	Ile	Ala	Asp	Ile	Asp	Ile	Glu	Ser
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Glu	Arg	Leu	Arg	Ser	Ile	Gly	Ala	Gln	Arg	Phe	Thr	Leu	Trp	Ala	Ile
	210					215					220				
Lys	Arg	Leu	Ile	Gly	Leu	Arg	Ser	Tyr	Lys	Gly	Arg	Val	Ser	Tyr	Leu
225					230					235					240
Leu	Gly	Lys	Gly	Lys	Lys	Glu	Pro	Pro	Val	Glu	Ala	Ala	Arg	Glu	Leu
				245					250					255	
Pro	Ala	Glu	Ser	Thr	Ala	Ala	Gly	Ile	Arg	Ser	Ser	Leu	Pro	Leu	Asn
		260					265						270		
Ala	Gly	Glu	Phe	His	Asp	Leu	Pro	Glu	Glu	Glu	Glu	Gly	Glu	Ala	Val
	275						280					285			
Leu	Asp	Gly	Glu	Gln	Phe	Ala	Asp	Ala	Ile	Ser	Leu	Asp	Arg	Ser	Val
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Tyr	Arg	Gln	His	Ala	Asp	Ser	Trp	His	Ser	Ala	Met	Ser	Arg	Arg	Thr
305					310					315					320
Ala	Tyr	Tyr	Ser	Leu	Gly	Gly	Pro	Ser	Met	Arg	Ser	Asn	Arg	Ser	Arg
			325						330					335	
Met	Ser	Ile	Ser	Gln	Arg	Ile	Glu	Ala	Asn	Ala	Glu	Phe	Ala	Glu	
			340					345				350			
Arg	Val	Pro	Thr	Gly	Thr	Ile	Pro	Pro	Leu	Gln	Met	Pro	Leu	Leu	Ser
		355					360					365			
Ser	Asp	Gly	Trp	Ile	Cys	Glu	Asp	Gly	Asp	Phe	Val	Met	Val	His	Ala
	370					375					380				
Ala	Tyr	Thr	Thr	His	Leu	Ser	Ser	Asp	Val	Phe	Phe	Ala	Pro	Glu	Ser
385					390					395					400
Arg	Leu	Asp	Asp	Gly	Leu	Ile	Tyr	Leu	Val	Ile	Ile	Arg	Arg	Gly	Val
				405					410					415	

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Ser Arg His Gln Leu Leu Asn Phe Met Leu Asn Leu Asn Ala Gly Thr  
 420 425 430  
 His Leu Pro Ile Gly Glu Asp Pro Phe Ile Lys Val Val Pro Cys Arg  
 435 440 445  
 Ala Phe Arg Ile Glu Pro Ser Ser Ser Asp Gly Ile Leu Val Val Asp  
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 Gly Glu Arg Val Glu Tyr Gly Pro Ile Gln Ala Glu Val Met Pro Gly  
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 Phe Val Ala Pro Thr Val Asp Glu Arg Arg Arg Arg Val Leu Val Leu  
 35 40 45  
 Leu Asn Pro Lys Ser Gly Ser Gly Asp Ala Arg Glu Val Phe Asn Met  
 50 55 60  
 His Val Thr Pro Val Leu Asn Glu Ala Glu Val Pro Tyr Asp Leu Tyr  
 65 70 75 80  
 Val Thr Lys His Ser Asn Phe Ala Ile Glu Phe Leu Ser Thr Arg Cys  
 85 90 95  
 Leu Asp Ala Trp Cys Cys Val Val Ala Val Gly Gly Asp Gly Leu Phe  
 100 105 110  
 His Glu Ile Val Asn Gly Leu Leu Gln Arg Gln Asp Trp Ala His Val  
 115 120 125  
 Leu Pro His Leu Ala Leu Gly Ile Ile Pro Cys Gly Ser Gly Asn Gly  
 130 135 140  
 Leu Ala Arg Ser Ile Ala His Cys Tyr Asn Lys Pro Val Leu Gly Ala  
 145 150 155 160  
 Ala Leu Thr Val Ile Ser Gly Arg Ser Ser Pro Met Asp Val Val Arg  
 165 170 175  
 Val Gln Leu Gln Ser Arg Ser Leu Tyr Ser Phe Leu Ser Ile Gly Trp  
 180 185 190  
 Gly Leu Ile Ser Asp Val Asp Ile Glu Ser Glu Arg Ile Arg Met Leu  
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 Gly Tyr Gln Arg Phe Thr Val Trp Thr Leu Tyr Arg Leu Val Asn Leu  
 210 215 220  
 Arg Thr Tyr Asn Gly Arg Ile Ser Tyr Leu Leu Thr Asp His Glu Val  
 225 230 235 240  
 Ser Ser Thr His Ser Ala Thr Gly Tyr Ala Ala Gln Arg Arg Met Gln  
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 Ser Ser Arg Ser Cys Asn Thr His Ile Asp Met Leu Asn Gly Pro Ala  
 260 265 270  
 Pro Ile Tyr His Ser Ser Ala Glu Tyr Leu Pro Gln Glu Phe Ala Asp  
 275 280 285

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Val Ile Ser Leu Glu Thr Ser Ile Asn Gln Ser Phe Arg Ser Arg Cys  
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 Asp Ser Trp Leu Ser Gly Gly Ser Arg Arg Ser Phe Tyr Tyr Ser Ile  
 305 310 315 320  
 Ser Glu Ser Ile Tyr His Ser Leu Ala Asp Glu Ser Glu Phe Ala Gly  
 325 330 335  
 Leu Ala Ala Ala Ser Leu Glu Asn Arg Gln Gln Asn Tyr Gly Pro Ala  
 340 345 350  
 Ser Glu Leu Pro Asp Leu Asn Glu Pro Leu Ser Glu Asp Gln Gly Trp  
 355 360 365  
 Leu Val Glu Glu Gly Glu Phe Val Met Met His Ala Val Tyr Gln Thr  
 370 375 380  
 His Leu Gly Ile Asp Cys His Phe Ala Pro Lys Ala Gln Leu Asn Asp  
 385 390 395 400  
 Gly Thr Ile Tyr Leu Ile Leu Ile Arg Ala Gly Ile Ser Arg Pro His  
 405 410 415  
 Leu Leu Ser Phe Leu Tyr Asn Met Ser Ser Gly Thr His Leu Pro Glu  
 420 425 430  
 Ser His Asp Asp His Val Lys Val Leu Pro Val Arg Ala Phe Arg Leu  
 435 440 445  
 Glu Pro Tyr Asp Asn His Gly Ile Ile Thr Val Asp Gly Glu Arg Val  
 450 455 460  
 Glu Phe Gly Pro Leu Gln Ala Glu Val Leu Pro Gly Ile Ala Arg Val  
 465 470 475 480  
 Met Val Pro Asn Val Ser Thr Phe Arg Phe Gln Ser Ala Thr Leu Gln  
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 His Gly Ile Pro Val Cys Ile Pro Val Arg Lys Arg Phe Val Leu Tyr  
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 Phe Thr Leu Met Leu Thr Glu Arg Arg Asn His Ala Arg Glu Leu Val  
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 Arg Ser Glu Glu Leu Gly Arg Trp Asp Ala Leu Val Val Met Ser Gly  
 50 55 60  
 Asp Gly Leu Met His Glu Val Val Asn Gly Leu Met Glu Arg Pro Asp  
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 Trp Glu Thr Ala Ile Gln Lys Pro Leu Cys Ser Leu Pro Ala Gly Ser  
 85 90 95  
 Gly Asn Ala Leu Ala Ala Ser Leu Asn His Tyr Ala Gly Tyr Glu Gln  
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 Val Thr Asn Glu Asp Leu Leu Thr Asn Cys Thr Leu Leu Leu Cys Arg  
 115 120 125

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Leu	Arg	Leu	Phe	Ser	Val	Leu	Ser	Leu	Ala	Trp	Gly	Phe	Ile	Ala	Asp
145					150					155					160
Val	Asp	Leu	Glu	Ser	Glu	Lys	Tyr	Arg	Arg	Leu	Gly	Glu	Met	Arg	Phe
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Thr	Leu	Gly	Thr	Phe	Leu	Arg	Leu	Ala	Ala	Leu	Arg	Thr	Tyr	Arg	Gly
			180					185					190		
Arg	Leu	Ala	Tyr	Leu	Pro	Val	Gly	Arg	Val	Gly	Ser	Lys	Thr	Pro	Ala
	195						200					205			
Ser	Pro	Val	Val	Val	Gln	Gln	Gly	Pro	Val	Asp	Ala	His	Leu	Val	Pro
	210					215					220				
Leu	Glu	Glu	Pro	Val	Pro	Ser	His	Trp	Thr	Val	Val	Pro	Asp	Glu	Asp
225					230					235					240
Phe	Val	Leu	Val	Leu	Ala	Leu	Leu	His	Ser	His	Leu	Gly	Ser	Glu	Met
				245					250					255	
Phe	Ala	Ala	Pro	Met	Gly	Arg	Cys	Ala	Ala	Gly	Val	Met	His	Leu	Phe
			260					265					270		
Tyr	Val	Arg	Ala	Gly	Val	Ser	Arg	Ala	Met	Leu	Leu	Arg	Leu	Phe	Leu
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Ala	Met	Glu	Lys	Gly	Arg	His	Met	Glu	Tyr	Glu	Cys	Pro	Tyr	Leu	Val
	290					295				300					
Tyr	Val	Pro	Val	Val	Ala	Phe	Arg	Leu	Glu	Pro	Lys	Asp	Gly	Lys	Gly
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Val	Phe	Ala	Val	Asp	Gly	Glu	Leu	Met	Val	Ser	Glu	Ala	Val	Gln	Gly
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Gln	Val	His	Pro	Asn	Tyr	Phe	Trp	Met	Val	Ser	Gly	Cys	Val	Glu	Pro
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Pro	Pro	Ser	Trp	Lys	Pro	Gln	Gln	Met	Pro	Pro	Pro	Glu	Glu	Pro	Leu
		355					360					365			

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